

WE CLAIM:

5 1. A method for enhancing sexual desire and responsiveness in a female individual, comprising orally administering to the individual a therapeutically effective amount of an orally active androgenic agent on an as-needed basis without regular dosing within the context of a chronic dosage regimen.

10 2. The method of claim 1, wherein the androgenic agent is contained within an oral dosage form.

15 3. The method of claim 2, wherein the pharmaceutical formulation is comprised of an immediate release dosage form, and the androgenic agent is administered about 0.25 to 72 hours prior to sexual activity.

20 4. The method of claim 3, wherein the androgenic agent is administered about 0.5 to 48 hours prior to anticipated sexual activity.

25 5. The method of claim 4, wherein the androgenic agent is administered about 1 to 24 hours prior to anticipated sexual activity.

6. The method of claim 5, wherein the androgenic agent is administered about 1 to 12 hours prior to anticipated sexual activity.

7. The method of claim 6, wherein the androgenic agent is administered about 1 to 4 hours prior to anticipated sexual activity.

8. The method of claim 2, wherein the pharmaceutical formulation is comprised of a sustained release dosage form.

SUB  
A2

TO  
B2  
Cont

9. The method of claim 8, wherein following administration, the sustained release dosage form provides release of the androgenic agent over a drug delivery period in the range of about 4 to 72 hours.

10. The method of claim 9, wherein the drug delivery period is in the range of about 4 to 48 hours.

11. The method of claim 10, wherein the drug delivery period is in the range of about 4 to 24 hours.

12. The method of claim 2 wherein the androgenic agent is selected from the group consisting of orally active testosterone esters, orally active dihydrotestosterone esters, methyl testosterone, dehydroepiandrosterone, and combinations thereof.

15            13. The method of claim 12, wherein the androgenic agent is an orally active testosterone ester.

14. The method of claim 13, wherein the orally active testosterone ester is selected from the group consisting of testosterone propionate, testosterone undecanoate, and testosterone C<sub>4</sub>-C<sub>6</sub> alkyl-substituted cycloalkylcarboxylates.

15. The method of claim 14, wherein the orally active testosterone ester is testosterone propionate.

25            16. The method of claim 12, wherein the androgenic agent is an orally active dihydrotestosterone ester.

17. The method of claim 16, wherein the orally active dihydrotestosterone ester is selected from the group consisting of dihydrotestosterone propionate, dihydrotestosterone undecanoate, and dihydrotestosterone C<sub>4</sub>-C<sub>6</sub> alkyl-substituted cycloalkylcarboxylates.

FOUO - FRODO  
Sub B2

18. The method of claim 17, wherein the orally active dihydrotestosterone ester is dihydrotestosterone propionate.

5 19. The method of claim 12, wherein the androgenic agent is selected from the group consisting of testosterone decanoate, testosterone pentadecanoate, testosterone undecanoate, testosterone pelargonate, testosterone tridecanoate, testosterone palmitate, testosterone caprate, testosterone isocaprate, testosterone  $\alpha$ -methylcaprate, testosterone  $\beta$ -methylcaprate, testosterone laurate, testosterone  $\alpha$ -methylpelargonate, testosterone  $\beta$ -methylpelargonate, testosterone  $\beta,\beta$ -dimethylpelargonate, testosterone  $\beta$ -(p-methyl-cyclohexyl)propionate, testosterone  $\beta$ -( $\beta$ -ethyl-cyclohexyl)-propionate, testosterone  $\beta$ -(cycloheptyl)-propionate, testosterone  $\alpha$ -methyl- $\beta$ -cyclohexyl propionate, testosterone  $\beta$ -methyl- $\beta$ -cyclohexyl propionate, testosterone cyclododecylcarboxylate, testosterone adamantine-1'-carboxylate, testosterone adamant-1'-yl-acetate, testosterone methyl- $\beta$ -cyclohexyl propionate, testosterone  $\beta$ -(bicyclo-[2,2,2-oct-1'-yl)-propionate, dihydrotestosterone decanoate, dihydrotestosterone pentadecanoate, dihydrotestosterone undecanoate, dihydrotestosterone pelargonate, dihydrotestosterone tridecanoate, dihydrotestosterone palmitate, dihydrotestosterone caprate, dihydrotestosterone isocaprate, dihydrotestosterone  $\alpha$ -methylcaprate, dihydrotestosterone  $\beta$ -methylcaprate, dihydrotestosterone laurate, dihydrotestosterone  $\alpha$ -methylpelargonate, dihydrotestosterone  $\beta$ -methylpelargonate, dihydrotestosterone  $\beta,\beta$ -dimethylpelargonate, dihydrotestosterone  $\beta$ -(p-methyl-cyclohexyl)propionate, dihydrotestosterone  $\beta$ -( $\beta$ -ethyl-cyclohexyl)-propionate, dihydrotestosterone  $\beta$ -(cycloheptyl)-propionate, dihydrotestosterone  $\alpha$ -methyl- $\beta$ -cyclohexyl propionate, dihydrotestosterone  $\beta$ -methyl- $\beta$ -cyclohexyl propionate, dihydrotestosterone cyclododecylcarboxylate, dihydrotestosterone adamantine-1'-carboxylate, dihydrotestosterone adamant-1'-yl-acetate, dihydrotestosterone methyl- $\beta$ -cyclohexyl propionate, dihydrotestosterone  $\beta$ -(bicyclo-[2,2,2-oct-1'-yl)-propionate, and combinations thereof.

Sub B2  
continued

20. The method of claim 19, wherein the dosage form further includes a lipoidal carrier effective to enhance the oral bioavailability of the androgenic agent.

21. The method of claim 1, wherein the therapeutically effective amount is in the range of about 1  $\mu$ g to about 250 mg.

22. The method of claim 21, wherein the therapeutically effective amount is in the range of about 1  $\mu$ g to about 150 mg.

23. The method of claim 22, wherein the therapeutically effective amount is in the range of about 10  $\mu$ g to about 100 mg.

24. The method of claim 2, wherein the therapeutically effective amount of the androgenic agent in the dosage form is a unit dosage.

25. The method of claim 1, further comprising administering a therapeutically effective amount of at least one additional active agent.

26. The method of claim 25, wherein the at least one additional active agent is administered with the androgenic agent.

27. The method of claim 25, wherein the at least one additional active agent is administered prior to administration of the androgenic agent.

28. The method of claim 25, wherein the at least one additional active agent is administered after administration of the androgenic agent.

29. The method of claim 25, wherein the at least one additional active agent is a vasoactive agent.

Sub B  
Cont

THESE ARE THE

SUB  
A3

30. The method of claim 29, wherein the vasoactive agent is a vasodilator.

31. The method of claim 30, wherein the vasodilator is selected from the group consisting of vasoactive prostaglandins, endothelin-derived relaxation factors, vasoactive intestinal polypeptide agonists, smooth muscle relaxants, leukotriene inhibitors, and pharmacologically active salts, esters, prodrugs, and metabolites thereof, and combinations of any of the foregoing.

32. The method of claim 31, wherein the vasodilator is a vasoactive prostaglandin.

33. The method of claim 32, wherein the vasoactive prostaglandin is selected from the group consisting of naturally occurring prostaglandins, semisynthetic prostaglandins, synthetic prostaglandins, and pharmaceutically acceptable, pharmacologically active salts, esters, amides, inclusion complexes, prodrugs, metabolites, and analogs thereof, and combinations of any of the foregoing.

34. The method of claim 33, wherein the vasoactive prostaglandin is selected from the group consisting of naturally occurring prostaglandins and hydrolyzable lower alkyl esters thereof.

35. The method of claim 34, wherein the vasoactive prostaglandin is selected from the group consisting of PGE<sub>0</sub>, PGE<sub>1</sub>, 19-hydroxy-PGE<sub>1</sub>, PGE<sub>2</sub>, 19-hydroxy-PGE<sub>2</sub>, PGA<sub>1</sub>, 19-hydroxy-PGA<sub>1</sub>, PGA<sub>2</sub>, 19-hydroxy-PGA<sub>2</sub>, PGB<sub>1</sub>, 19-hydroxy-PGB<sub>1</sub>, PGB<sub>2</sub>, 19-hydroxy-PGB<sub>2</sub>, PGB<sub>3</sub>, PGD<sub>2</sub>, PGF<sub>1α</sub>, PGF<sub>2α</sub>, PGE<sub>3</sub>, PGF<sub>3α</sub>, PGI<sub>2</sub>, and hydrolyzable lower alkyl esters thereof.

36. The method of claim 35, wherein the vasoactive prostaglandin is selected from the group consisting of PGE<sub>0</sub>, PGE<sub>1</sub>, PGE<sub>2</sub>, and the methyl, ethyl and isopropyl esters thereof.

Sub B2  
Cont  
T O C : T E N O C

37. The method of claim 32, wherein the vasoactive prostaglandin is selected from the group consisting of arboprostil, carbaprostacyclin, carboprost tromethamine, dinoprost tromethamine, dinoprostone, enprostil, iloprost, lipoprost, gemeprost, metenoprost, sulprostone, tiaprost, viprostil, viprostil methyl ester, 16,16-dimethyl- $\Delta^2$ -PGE<sub>1</sub> methyl ester, 15-deoxy-16-hydroxy-16-methyl-PGE<sub>1</sub> methyl ester, 16,16-dimethyl-PGE<sub>1</sub>, 11-deoxy-15-methyl-PGE<sub>1</sub>, 16-methyl-18,18,19,19-tetrahydro-carbacyclin, 16(RS)-15-deoxy-16-hydroxy-16-methyl-PGE<sub>1</sub> methyl ester, (+)-4,5-didehydro-16-phenoxy- $\alpha$ -tetranor-PGE<sub>2</sub> methyl ester, 11-deoxy-11 $\alpha$ ,16,16-trimethyl-PGE<sub>2</sub>, (+)-11 $\alpha$ ,16 $\alpha$ ,16 $\beta$ -dihydroxy-1,9-dioxo-1-(hydroxymethyl)-16-methyl-trans-prostene, 9-chloro-16,16-dimethyl-PGE<sub>2</sub>, 16,16-dimethyl-PGE<sub>2</sub>, 15(S)-15-methyl-PGE<sub>2</sub>, 9-deoxy-9-methylene-16,16-dimethyl-PGE<sub>2</sub>, potassium salt, 19(R)-hydroxy-PGE<sub>2</sub>, 11-deoxy-16,16-dimethyl-PGE<sub>2</sub>, and combinations thereof.

38. The method of claim 32, wherein the therapeutically effective amount of the vasodilator is in the range of approximately 1 to 5000  $\mu$ g.

39. The method of claim 38, wherein the therapeutically effective amount of the vasodilator is in the range of approximately 20 to 2000  $\mu$ g.

40. The method of claim 25, wherein the at least one additional active agent is selected from the group consisting of rho kinase inhibitors, melanocortin peptides, endothelin antagonists, growth factors and other peptidyl drugs; selective androgen receptor modulators (SARMs), neuropeptides, amino acids, serotonin agonists, serotonin antagonists, calcium channel blockers, potassium channel openers; potassium channel blockers, dopamine agonists, dopamine antagonists, non-androgenic steroids, and combinations thereof.

41. The method of claim 40, wherein the additional active agent is a dopamine agonist.

sub B cont  
T0220 T0200

42. The method of claim 41, wherein the dopamine agonist is selected from the group consisting of levodopa, bromocriptine, pergolide, apomorphine, piribedil, pramipexole, ropinirole, and combinations thereof.

5  
SUB  
A4  
43. The method of claim 25, wherein administration of the at least one additional active agent is topical, transdermal, sublingual, intranasal, buccal, rectal, parenteral, or by inhalation.

10  
44. A method for enhancing sexual desire and responsiveness in a female individual, comprising orally administering to the individual, approximately 0.25 to 72 hours prior to sexual activity, a therapeutically effective amount of an orally active androgenic agent, followed by topical administration, approximately 0.25 to 24 hours prior to sexual activity, of a therapeutically effective amount of a prostaglandin.

15  
45. The method of claim 44, wherein the prostaglandin is selected from PGE<sub>0</sub>, PGE<sub>1</sub>, PGE<sub>2</sub>, and hydrolyzable lower alkyl esters thereof.

20  
46. A method for maintaining improving the tissue health of the female genitalia, comprising orally administering to a female individual a therapeutically effective amount of an orally active androgenic agent on an as-needed basis without regular dosing within the context of a chronic dosage regimen.

25  
47. A method for preventing vaginal atrophy, comprising orally administering to a female individual a therapeutically effective amount of an orally active androgenic agent on an as-needed basis without regular dosing within the context of a chronic dosage regimen.

30  
SUB  
A5  
48. A method for preventing vaginal pain during sexual intercourse, comprising orally administering to a female individual suffering from dyspareunia a therapeutically

effective amount of an orally active androgenic agent on an as-needed basis without regular dosing within the context of a chronic dosage regimen.

SUB  
P5  
5 49. A method for alleviating vaginal itching and dryness, comprising orally administering to a female individual in need of such treatment a therapeutically effective amount of an orally active androgenic agent on an as-needed basis without regular dosing within the context of a chronic dosage regimen.

10 50. A method for enhancing sexual desire and responsiveness in a female individual, comprising orally administering an orally active androgenic agent to the individual in an amount effective to provide a blood level of the agent or a metabolite thereof that approximates the blood level of the agent or a metabolite thereof during ovulation, wherein said administering is on an as-needed basis without regular dosing within the context of a chronic dosage regimen.

15 51. An oral dosage form to enhance female sexual desire and responsiveness, comprising (a) approximately 1  $\mu$ g to about 150 mg of testosterone propionate, (b) a pharmaceutically acceptable carrier suitable for oral drug administration and selected to provide immediate release of the androgenic agent from the formulation following oral administration.

20 52. The dosage form of claim 51, comprising approximately 10  $\mu$ g to about 100 mg testosterone propionate.

25 53. An oral dosage form to enhance female sexual desire and responsiveness, comprising (a) approximately 1  $\mu$ g to about 150 mg of testosterone propionate, (b) a pharmaceutically acceptable carrier suitable for oral drug administration and selected to provide sustained release of the testosterone propionate over an extended drug delivery period in the range of about 4 hours to 72 hours.

30

RECEIVED



packaged kit for  
comprising  
ally active an  
to administ  
I desire and

Ad  
Me